PATENT SPECIFICATION

810,108

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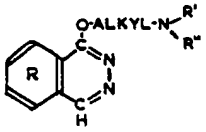
COMPLETE SPECIFICATION

Phthalazine Compounds Basically Substituted in the 1-Position

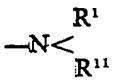
We, CASSELLA FARBWERKE MAINKUR AKTIENGESELLSCHAFT, a body corporate organised under the laws of Germany, of 16 Frankfurt / M.-Fechenheim, Germany, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention is concerned with phthalazine compounds basically substituted in the 1-position and with a process for the production thereof.

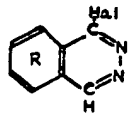
According to the invention, phthalazine compounds basically substituted in the 1-position and corresponding to the general formula:—



wherein in the 4-position and/or in the benzene nucleus R there may be present substituents which do not react with alkali metal compounds of hydroxy-alkyl-amines, and



is the residue of tertiary amine, are produced by reacting an alkali metal compound of a tertiary hydroxyalkyl-amine with a 1-halogen-phthalazine of the general formula:—



wherein Hal is a halogen atom and wherein in the 4-position and/or in the benzene nucleus R there may be present substituents which do not react with alkali metal compounds of hydroxy-alkyl-amines.

They are distillable oils or crystalline compounds and form, with acids, stable water-soluble salts from which they are separated by concentrated alkali lye. They exhibit valuable therapeutic activity.

Similar compounds to those of the present invention are described and claimed in our Specification No. 23777/56 (Serial No. 808,636) but the compounds of this latter specification differ from those of the present invention in that the basic alkyl group is in the 2-position instead of the 1-position.

Examples of the basically substituted alcohols which may be used for the preparation of the new compounds according to the present invention are diethylaminoethanol, dibutylaminoethanol, N-hydroxy ethylpiperidine, N-hydroxyethylpyrrolidine, N-hydroxyethylmorpholine, 1 - dimethylamino-2-propanol, and hydroxyethylmethylaniline.

The basically substituted heterocycles thus obtained may be used as such or in the form of their hydrochlorides, hydrobromides, sulphates or the salts with organic acids, such as, for example, benzoic acid, picric acid, citric acid, and gentisic acid. They possess at a favourable therapeutic index and a valuable antiphlogistic and analgesic action.

The following Examples are given for the purpose of illustrating the invention, the parts being by weight and all temperatures in degrees Centigrade.

EXAMPLE 1.

83 parts of 1-chlorophthalazine (obtained by a treatment of 1-oxo-1.2-dihydrophthalazine with phosphorus oxychloride) are dissolved in 600 parts of benzene at 20°C. The filtered solution flows at 20—30°C. within one hour to a solution previously prepared from 11.5 parts of sodium in 250 parts of diethylaminoethanol. The temperature may be maintained as a constant level by a slight cooling. After

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the admission is completed, the reaction mixture is stirred for some 3 hours at 80°C. Upon cooling, the sodium chloride is removed by filtering with suction, and benzene as well as diethylaminoethanol in excess is distilled off under reduced pressure. The residue is distilled at about 1 mm. Hg. (boiling point 150—155° C.). The viscous yellowish oil with a refractive index $N_D25°$ 1.5570 represents the 1-(diethylamino-ethoxy)-phthalazine. It forms a dihydrochloride of a melting point of 148°C. (from propylalcohol) and a picrate of a melting point of 140—141°C.

EXAMPLE 2.

83 parts of 1-chloro-phthalazine are dissolved in 600 parts of benzene. The filtered solution flows at 35—40°C. into a solution of 11.5 parts of sodium in 250 parts of dimethylaminoethanol. The reaction mixture is stirred for 3 hours at 80°C. and, after removing the sodium chloride, the mass is distilled. An oil is thus obtained which boils at 0.75 mm. Hg. and 150°C. and which forms a picrate of a melting point of 150—152°C. The compound is the 1-(dimethylaminoethoxy)-phthalazine.

EXAMPLE 3.

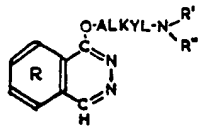
By combining a solution of 83 parts of 1-chlorophthalazine in benzene with a solution of 11.5 parts of sodium in 250 parts of dibutylaminoethanol and heating the mixture for 3 hours at 80°C., the procedure of distillation yields 1-(dibutylaminoethoxy)-phthalazine of a boiling point of 175°C. at 0.4 mm. Hg. The picrate melts at 125°C., the dihydrochloride at 107—108°C.

EXAMPLE 4.

4 parts of sodium are dissolved in 100 parts of diethylaminoethanol. While stirring, 27 parts of 1 - chloro-4-methylphthalazine, (obtained according to Gabriel, "Berichte der deutschen chemischen Gesellschaft" *26*, p. 708) dissolved in 500 parts of benzene are added to 30°C. during 1 hour. The mixture is stirred for a further two hours at 80°C. and the reaction product separated by distillation. The 1-(diethylaminoethoxy) - 4 - methylphthalazine thus obtained boils under a pressure of 0.7 mm. Hg. at 170—173°C. and forms a dihydrochloride of m.p. 175—176°C.

WHAT WE CLAIM IS:—

1. New basically substituted phthalazine compounds, and salts thereof, of the general formula:—



wherein in the 4-position and/or in the benzene nucleus R there may be present substituents which do not react with alkali metal compounds of hydroxy-alkylamines and

$$-N<^{R^1}_{R^{11}}$$

is the residue of a tertiary amine.

2. Salts of the phthalazine compounds of the general formula given in claim 1, wherein the acid used is hydrochloric, hydrobromic, sulphuric, benzoic, picric, citric or gentisic acid.

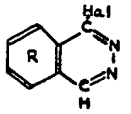
3. 1-(diethylaminoethoxy)-phthalazine and the dihydrochloride and picrate thereof.

4. 1-(dimethylaminoethoxy)-phthalazine and the picrate thereof.

5. 1-(dibutylaminoethoxy)-phthalazine and the dihydrochloride and picrate thereof.

6. 1-(diethylaminoethoxy)-4-methylphthalazine and the dihydrochloride thereof.

7. A process of preparing phthalazine compounds of the general formula given in claim 1, wherein an alkali metal compound of a tertiary hydroxy-alkylamine is reacted with a 1 - halogen - phthalazine of the general formula:—



8. A process of preparing phthalazine compounds basically substituted in the 1-position substantially as described in any one of the foregoing Examples.

9. Basically substituted phthalazine compounds of the general formula given in claim 1, whenever prepared by the process according to claim 8 or 9.

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